Differential trafficking of AMPA and NMDA receptors by SAP102 and PSD-95 underlies synapse development.

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Public Summary:

Scientific Abstract:
The development of glutamatergic synapses involves changes in the number and type of receptors present at the postsynaptic density. To elucidate molecular mechanisms underlying these changes, we combine in utero electroporation of constructs that alter the molecular composition of developing synapses with dual whole-cell electrophysiology to examine synaptic transmission during two distinct developmental stages. We find that SAP102 mediates synaptic trafficking of AMPA and NMDA receptors during synaptogenesis. Surprisingly, after synaptogenesis, PSD-95 assumes the functions of SAP102 and is necessary for two aspects of synapse maturation: the developmental increase in AMPA receptor transmission and replacement of NR2B-NMDARs with NR2A-NMDARs. In PSD-95/PSD-93 double-KO mice, the maturational replacement of NR2B- with NR2A-NMDARs fails to occur, and PSD-95 expression fully rescues this deficit. This study demonstrates that SAP102 and PSD-95 regulate the synaptic trafficking of distinct glutamate receptor subtypes at different developmental stages, thereby playing necessary roles in excitatory synapse development.

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